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Disquieted by Experience: Noise, the Amygdala, and Anxiety-like Responses in Mice

Lindsey Konkel Neabore

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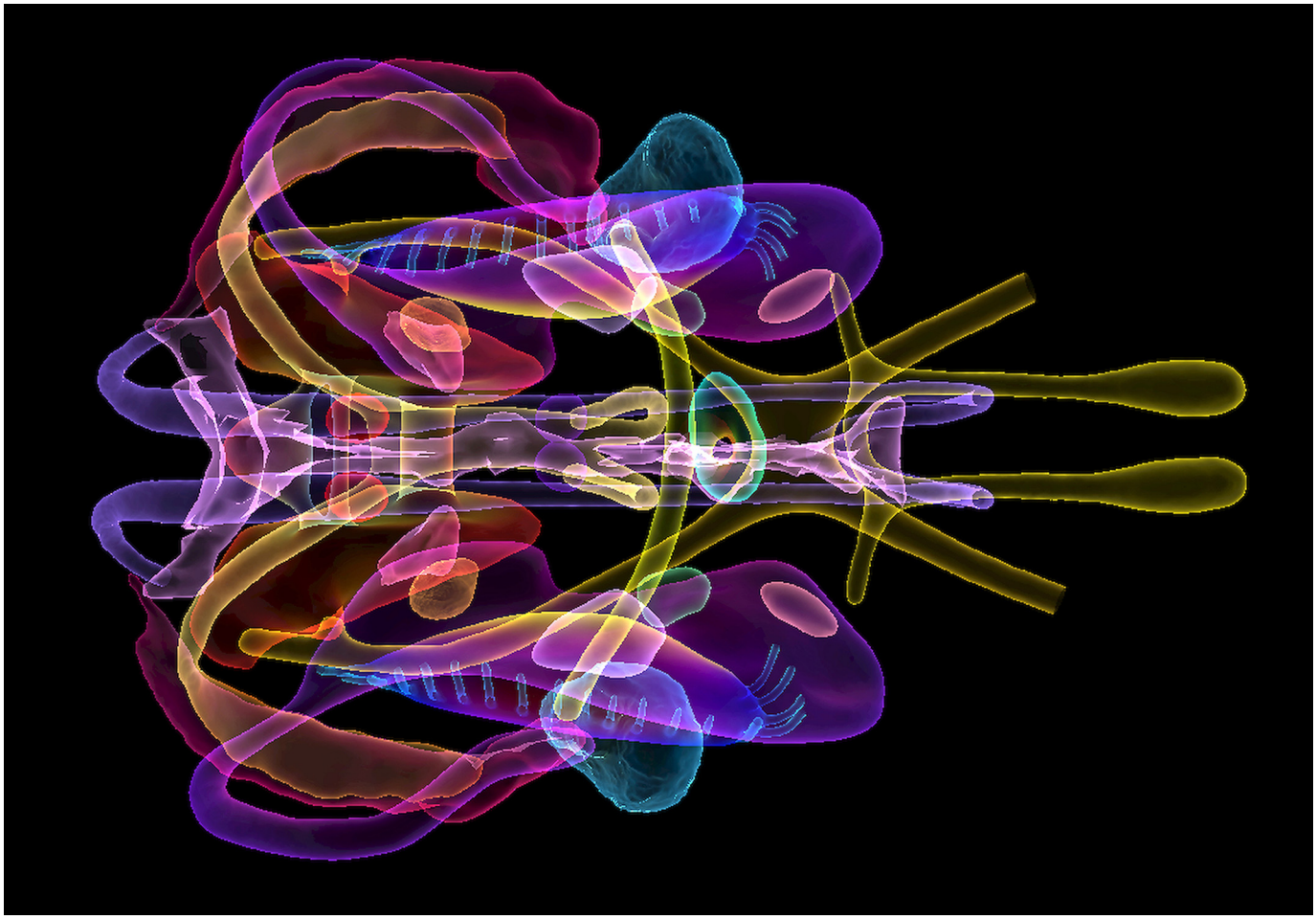
It is well known that exposure to loud noises can lead to hearing loss,[1] but a growing body of research shows that chronic exposure to noise at lower levels may harm the body in other, less obvious, ways. Moderate levels of traffic noise have been associated with increased risks for heart disease and other cardiometabolic diseases, including stroke, diabetes, and obesity—all at levels safe for hearing.[2,3] Stress and sleep disturbances also have been linked to moderate levels of environmental (as opposed to occupational) noise.[4,5]

Now, an experimental study published in *Environmental Health Perspectives* finds that chronic exposure to moderate levels of noise can cause anxiety-like behaviors in rodents through changes to the amygdala, part of the brain's emotion-processing system.[6] The authors wanted to learn more about the effects of chronic moderate noise on emotional disorders because city residents had complained of anxiety brought on by daily traffic noise, according to the research team. The work was led by Xiaoqi Peng of the University of Science and Technology of China in Hefei.

The exposure limit set by the U.S. National Institute for Occupational Safety and Health to prevent hearing loss in the workplace is an 8-hour average of 85 dB (for comparison, lawnmowers and subway trains are in the range of 85–100 dB).[7] Most of us do not live or work in environments with noise levels above that threshold, explains corresponding author Zhi Zhang, also of the University of Science and Technology of China. Exposures to moderate noise, or less than 85 dB, are more common.[6] For instance, a 2015 study in New York City found across all five boroughs a mean street noise level of 73.4 dB, although there was substantial spatial variation.[8]

The researchers exposed adult male mice to chronic moderate white noise (85 dB, 4 hours per day) for 4 weeks. Afterward, they observed the mice in various behavioral tests. Noise-exposed mice showed more anxiety-like behaviors—including avoidance of new spaces and situations—than did unexposed mice. Surprisingly, says Zhang, the noise-exposed mice also showed greater sensitivity to later acute noise exposures. Even after 4 weeks without noise, chronically exposed mice exhibited anxiety-like behaviors upon



The new study implicates the amygdala in noise-induced anxiety-like behaviors in mice. The human amygdala appears as two rounded shapes colored light blue (top and bottom center) in this three-dimensional magnetic resonance imaging scan of the brain's limbic system. Image: © K H Fung/Science Source.

exposure to just 2 hours of white noise at 75–85 dB. This similar but shorter exposure did not cause behavior changes in control mice.

To understand the neural processes underpinning the findings, the researchers studied the animals using a range of techniques, including molecular analyses of brain tissue. Using viral tracing, the researchers identified the brain circuitry involved in noise-induced anxiety-like behaviors. Then, they manipulated that circuitry by using optogenetic excitation to evoke the behaviors, and chemogenetic inactivation to abolish the behaviors. Their findings showed that chronic noise was transmitted from the auditory brain regions to the amygdala and that an overstimulated amygdala elicited anxiety-like behaviors in these mice. It is the first study to examine the involvement of these circuits in noise-evoked anxiety, the researchers say.

Previous research in rodents using contextual fear conditioning has implicated the amygdala in noise-induced fear.[9] In such conditioning, pairing an innocuous sensory stimulus, such as a familiar sound, with a fear-inducing stimulus, such as a foot shock, can elicit a fearful response later upon application of just the innocuous stimulus. "The [new] paper shows strong evidence that the amygdala is [also] involved in noise-induced stress," says Wei Sun, an audiology researcher at the University at Buffalo who was not involved in the research.

The researchers highlight the study's insight into biological mechanisms that are technically challenging to evaluate in humans. The use of moderate, environmentally relevant exposure levels supports the relevance of the study to humans, says Richard Neitzel, an exposure scientist studying noise at the University of Michigan who also was not involved in the study.

That said, the relationship between noise and anxiety may be far more complex in humans than in mice, write the researchers. "An animal study gives you more control over [other contributing] factors," says Sun. In addition, human exposures tend to be more variable in terms of duration and level from day to day, explains Neitzel, so the experimental conditions tested in this study do not mirror human exposures. He adds that furthermore, because only adult male mice were studied, it is not clear whether exposures could have different impacts at different points in the life course, nor whether the use of only male mice limits the translatability of the findings. In humans, women are more than twice as likely to develop an anxiety disorder in their lifetime as men.[10]

Increasing evidence from epidemiological studies over the last 20 years[11] suggests moderate noise may be linked to stress, adverse mental health impacts, and decreased quality of life, says Charlotte Clark, an epidemiologist who studies health effects of environmental noise effects at St. George's University of London and who was not involved in the study. "We used to think you needed high levels of noise to see health effects," she says. "But it is becoming clear that we do not really know what levels are safe."

Lindsey Konkel Neabore is a New Jersey–based journalist who reports on science, health, and the environment.

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